IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	Confirmation No.
Li *et al.*	Art Unit: To Be Assigned
Appl. No. To Be Assigned (Continuation of App. No. 09/518,383)	Examiner: To Be Assigned
Filed: Herewith	Atty. Docket: 1488.1220003/EKS/EJH
For: **Human G-Protein Coupled Receptors**	

Preliminary Amendment

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

In advance of prosecution, please amend the application as follows.

In the Claims

Please cancel claims 1-21 (22 total claims, two claims were inadvertently listed as claim 4) without prejudice to or disclaimer of the subject matter thereof.

Please add the following claims 23-78:

-- 23. (New) An isolated antibody which specifically binds the polypeptide of SEQ ID NO:2.

24. (New) The antibody of claim 23, which specifically binds to the polypeptide of amino acids 1 to 342 of SEQ ID NO:2.

25. (New) The antibody of claim 24, which specifically binds to the polypeptide of amino acids 2 to 342 of SEQ ID NO:2.

26. (New) The antibody of claim 25, which specifically binds to the mature polypeptide produced upon cellular expression of the polypeptide of SEQ ID NO:2.

27. (New) The antibody of claim 23, wherein said antibody is polyclonal.

28. (New) The antibody of claim 23, wherein said antibody is monoclonal.

29. (New) The antibody of claim 28, wherein said antibody is produced by a method selected from the group consisting of the hybridoma technique, the trioma technique, the human B-cell hybridoma technique, and the EBV-hybridoma technique.

30. (New) The antibody of claim 29, wherein said antibody is produced by the hybridoma technique.

31. (New) The antibody of claim 29, wherein said antibody is produced by the trioma technique.

32. (New) The antibody of claim 27, wherein said antibody is produced by the human B-cell hybridoma technique.

33. (New) The antibody of claim 29, wherein said antibody is produced by the EBV-hybridoma technique.

34. (New) The antibody of claim 23, wherein said antibody is chimeric.

35. (New) The antibody of claim 23, wherein said antibody is humanized.

36. (New) The antibody of claim 23, wherein said antibody is produced in transgenic mice.

37. (New) The antibody of claim 23, wherein said antibody is a single-chain antibody.

38. (New) A composition comprising the antibody of claim 23, and a carrier.

39. (New) A method of producing the antibody of claim 23, comprising:

(a) introducing an immunogen into an animal; and

(b) recovering said antibody.

40. (New) An isolated antibody fragment which specifically binds to the polypeptide of SEQ ID NO:2.

41. (New) The antibody fragment of claim 40, which specifically binds to the polypeptide of amino acids 1 to 342 of SEQ ID NO:2.

42. (New) The antibody fragment of claim 41, which specifically binds to the polypeptide of amino acids 2 to 342 of SEQ ID NO:2.

43. (New) The antibody fragment of claim 42, which specifically binds to the mature polypeptide produced upon cellular expression of the polypeptide of SEQ ID NO:2.

44. (New) The antibody fragment of claim 40, wherein said antibody fragment comprises an Fab fragment.

45. (New) The antibody fragment of claim 40, wherein said antibody fragment comprises a single chain antibody fragment.

46. (New) The antibody fragment of claim 40, wherein said antibody fragment is chimeric.

47. (New) The antibody fragment of claim 40, wherein said antibody fragment is the product of an Fab expression library.

48. (New) The antibody fragment of claim 40, wherein said antibody fragment is fused to a heterologous polypeptide.

49. (New) A composition comprising the antibody fragment of claim 40, and a carrier.

50. (New) A method of producing the antibody fragment of claim 40, comprising:

(a) introducing an immunogen into an animal; and

(b) recovering said antibody fragment.

51. (New) An isolated antibody which specifically binds the polypeptide encoded by the human cDNA in ATCC Deposit No. 209003.

52. (New) The antibody of claim 51, which specifically binds to the mature polypeptide produced upon cellular expression of the polypeptide encoded by the human cDNA in ATCC Deposit No. 209003.

53. (New) The antibody of claim 51, wherein said antibody is polyclonal.

54. (New) The antibody of claim 51, wherein said antibody is monoclonal.

55. (New) The antibody of claim 54, wherein said antibody is produced by a method selected from the group consisting of the hybridoma technique, the trioma technique, the human B-cell hybridoma technique, and the EBV-hybridoma technique.

56. (New) The antibody of claim 55, wherein said antibody is produced by the hybridoma technique.

57. (New) The antibody of claim 55, wherein said antibody is produced by the trioma technique.

58. (New) The antibody of claim 55, wherein said antibody is produced by the human B-cell hybridoma technique.

59. (New) The antibody of claim 55, wherein said antibody is produced by the EBV-hybridoma technique.

60. (New) The antibody of claim 51, wherein said antibody is chimeric.

61. (New) The antibody of claim 51, wherein said antibody is humanized.

62. (New) The antibody of claim 51, wherein said antibody is produced in transgenic mice.

63. (New) The antibody of claim 51, wherein said antibody is a single-chain antibody.

64. (New) A composition comprising the antibody of claim 51, and a carrier.

65. (New) A method of producing the antibody of claim 51, comprising:

(a) introducing an immunogen into an animal; and

(b) recovering said antibody fragment.

66. (New) An isolated antibody fragment which specifically binds to the polypeptide encoded by the human cDNA in ATCC Deposit No. 209003.

67. (New) The antibody fragment of claim 66, which specifically binds to the mature polypeptide produced upon cellular expression of the polypeptide encoded by the human cDNA in ATCC Deposit No. 209003.

68. (New) The antibody fragment of claim 66, wherein said antibody fragment comprises an Fab fragment.

69. (New) The antibody fragment of claim 66, wherein said antibody fragment comprises a single chain antibody fragment.

70. (New) The antibody fragment of claim 66, wherein said antibody fragment is chimeric.

71. (New) The antibody fragment of claim 66, wherein said antibody fragment is the product of an Fab expression library.

72. (New) The antibody fragment of claim 66, wherein said antibody fragment is fused to a heterologous polypeptide.

73. (New) A composition comprising the antibody fragment of claim 66, and a carrier.

74. (New) A method of producing the antibody fragment of claim 66, comprising:

(a) introducing an immunogen into an animal; and

(b) recovering said antibody fragment.

75. (New) A method to screen for a compound which binds to a polypeptide comprising amino acids 2 to 342 of SEQ ID NO:2, comprising:

(a) contacting a compound to be screened with said polypeptide; and

(b) determining if said compound binds to said polypeptide.

76. (New) The method of claim 75, wherein said compound to be screened comprises a molecule selected from the group consisting of a small molecule, a peptide, a peptide-like molecule, a polypeptide, and an antibody.

77. (New) A method to screen for a compound which binds to the polypeptide encoded by the human cDNA in ATCC Deposit No. 209003, comprising:

(a) contacting a compound to be screened with said polypeptide; and

(b) determining if said compound binds to said polypeptide.

78. (New) The method of claim 77, wherein said compound to be screened comprises a molecule selected from the group consisting of a small molecule, a peptide, a peptide-like molecule, a polypeptide, and an antibody. --

Remarks

Upon entry of the foregoing amendment, claims 23-78 are pending in the application, with claims 23, 40, 51, 66, 75, and 77 being the independent claims. Support for added claims 23-78 may be found throughout the specification, in Figures 2 and 4, and in the attached copy of a Declaration under 37 C.F.R. § 1.132 by Steven M. Ruben (the Ruben Declaration) filed in conjunction with an Amendment and Reply filed with the grandparent case, Application No. 08/852,824 (the '824 Application), now, U.S. Patent No. 6,060,272. .

Except for priority data, and reformatting to conform to 37 C.F.R. § 1.52(b)(6), the specification submitted herewith is identical to the specification of the parent Application No. 09/518,383 (the '383 Application).

A 17-page Sequence Listing is submitted herewith. A computer readable form of the Sequence Listing is also attached. In accordance with 37 C.F.R. § 1.821(f), the paper copy of the Sequence Listing and the computer readable copy of the Sequence Listing submitted herewith in the above-mentioned application are the same.

Applicants hereby state that no new matter has been added by way of the foregoing amendments.

The Sequence Listing

The Sequence Listing submitted herewith corrects typographical errors present in the Sequence Listing originally filed with the '824 Application. The undersigned hereby states that the changes made in the Sequence Listing in the '824 Application do not include new matter.

Typographical errors were incorporated in the Sequence Listing originally filed with the '824 Application due to attorney error. The errors appeared in SEQ ID NO:1 through SEQ ID NO:4 of the Sequence Listing, and since copies of the Sequence Listing pages for SEQ ID NO:1 and SEQ ID NO:3 were used as informal drawings in Figures 1 and 3 as originally filed, the errors also appeared in those drawings. Applicants stress that these errors were incorporated during the drafting of the application, and that Applicants were in possession of the correct sequence at the time the application was filed. Support may be found, *inter alia*, in Figures 2 and 4, and in the attached copy of the Ruben Declaration. In particular, SEQ ID NO:1 as originally filed in the '824 Application contained typographical errors at the following nucleotide positions: position 242, which should be A rather than T; position 266, which should be C rather than A; position 1870, where a T should be deleted, and position 2206, where an N should be deleted. SEQ ID NO:2 as originally filed in the '824 Application contained typographical errors at the following amino acid positions: position 6, which should be Asn rather than Ile; and position 14, which should be Thr rather than Asn. The latter typographical errors in the amino acid sequence were also reflected in the amino acid sequence shown under the nucleotide sequence in SEQ ID NO:1 as originally filed in the '824 Application. SEQ ID NO:3 as originally filed in the '824 Application contained typographical errors at the following nucleotide positions: position 828, which

should be T rather than C; and position 831, which should be T rather than A. Note that this latter typographical error introduced a stop codon into the open reading frame, causing the amino acid sequence, as translated from the sequence with the typographical error, to stop at position 260. SEQ ID NO:4, therefore, was truncated at position 260, which should be Phe rather than Ser, and the translation should continue to amino acid 384. SEQ ID NO:4 as originally filed in the '824 Application contained typographical errors at the following amino acid positions: position 191, which should be Asp rather than Asn, position 202, which should be Lys rather than Arg, and position 204, which should be Tyr rather than Thr. In addition, the translation should start with the Met at position 1, rather than the Ala at position -16. The latter typographical errors in the amino acid sequence were also reflected in the amino acid sequence shown under the nucleotide sequence in SEQ ID NO:3 as originally filed in the '824 Application.

In support of the fact that Applicants indeed had the correct sequence at the time the '824 Application was filed, the sequence of SEQ ID NO:2, as amended, is shown in the top line of the alignment shown in Fig. 2, and the sequence of SEQ ID NO:4, as amended, is shown in the top line of the alignment shown in Fig. 4, except for five residues at the 3' end of the polypeptide. These latter five residues are not in the alignment simply because they did not align with the second sequence, *i.e.*, SEQ ID NO:18.

There is a line of chemical case law where applicants have been permitted to amend the specification to correct the formula of a chemical compound after an application's filing date provided that it had been demonstrated that one of skill in the art would have appreciated that the applicant was in possession of the compound itself at the time of filing. The rationale is that the formula is an inherent property of the compound and thus amending

the specification to correct the formula is not new matter. *See In re Nathan*, 140 U.S.P.Q. 601, 604 (C.C.P.A. 1964). *Accord Kennecott Corp. v. Kyocera Int'l, Inc.*, 5 U.S.P.Q.2d 1194, 1198 (Fed. Cir. 1987), *cert. denied*, 486 U.S. 1008 (1988) ("The disclosure in a subsequent patent application of an inherent property of a product does not deprive that product of the benefit of the earlier filing date.").

In the field of biotechnology, applicants often rely on a deposited clone, where the deposit was made prior to filing, to establish possession of claimed polynucleotides or proteins. The focus for determining whether applicants were in possession of these polynucleotides or proteins has been determined, at least in part, by considering whether the applicant has (1) established that one skilled in the art in possession of the deposited clone would have been aware of both the DNA sequence and the encoded amino acid sequence, or would be able to determine these sequences without undue experimentation, (2) established that the DNA and amino acids sequences are described in a manner such that one skilled in the art could distinguish them from other sequences, and (3) resequenced a clone which is identical to that of the deposit and established a "chain of custody" for this clone. *See e.g.*, *Ex parte Maizel,* 27 U.S.P.Q.2d 1662, 1669-1670 (B.P.A.I. 1992).

At paragraphs 8 and 14 of the attached copy of the Ruben Declaration, Dr. Ruben states that he is of the opinion that the correct EBI-2 and EDG-1-like nucleotide and amino acid sequences would have been apparent, as of the May 7, 1997 filing date of the '824 Application, to one skilled in the art in possession of ATCC Deposit Nos. 209003 and 209004 and the sequence data originally filed with the present application. Dr. Ruben bases this position on the facts that the correct EBI-2 and EDG-1-like coding sequences can be readily determined from the deposited clones, and methods for sequencing these clones were

routine in the art in May of 1997 (Ruben Declaration, paras. 8 and 14). Thus, the nucleotide sequences of these clones are chemical structures which are inherent properties of the clones. Further, the EBI-2 and EDG-1-like sequences are described in the present application in sufficient detail so that one skilled in the art could distinguish the claimed invention from other compounds.

The typographical errors present in the Sequence Listing as filed were incorporated into the '824 Application during drafting by the attorneys, and were not the errors of the Applicants. Indeed, at the time of filing of the '824 Application, Applicants possessed the nucleotide sequences SEQ ID NO:1 and SEQ ID NO:3 (as amended) of the two cDNA clones (HHPGS02 and HNFDL69) that encode the EBI-2 and EDG-1-like amino acid sequences of SEQ ID NO:2 and SEQ ID NO:4 (as amended) of the present application (Ruben Declaration, paras. 6-7 and 12-13). Applicants have also submitted evidence to establish that these clones are identical to those deposited at the ATCC and given Accession Nos. 209003 and 209004 (Ruben Declaration, paras. 4 and 10). Applicants have thus established a "chain of custody" which demonstrates that the nucleotide sequence data included in SEQ ID NO: 1 and SEQ ID NO:3 (as amended) of the present application was obtained from the clones deposited with the ATCC and given Accession Nos. 209003 and 209004.

In light of this information, the inclusion of the correct sequences present in the clones of ATCC Deposit Nos. 209003 and 209004, and in possession of the Applicants at the time of filing of the '824 Application, does not represent new matter.

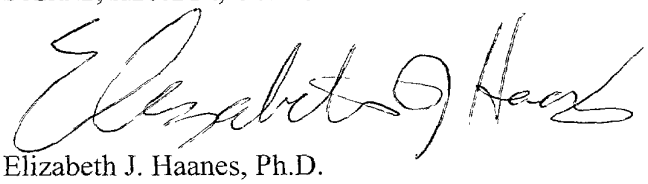
Summary

It is respectfully believed that this application is now in condition for examination. Early notice to this effect is respectfully requested

The U.S. Patent and Trademark Office is hereby authorized to charge any fee deficiency, or credit any overpayment, to our Deposit Account No. 19-0036.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.



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Version with markings to show changes made

Claims 1-21 are canceled (22 total claims, two claims were inadvertently listed as claim 4 in the original application).

Claims 23-78 are added.